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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/981,506	10/17/2001	Gregory R. Chiklis	19383-014	6911

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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	PAPER NUMBER
1648	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/981,506	CHIKLIS ET AL.	
	Examiner	Art Unit	
	Louise Humphrey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-11,13-63,65,66 and 68-71* is/are pending in the application.

4a) Of the above claim(s) *5-11,16-48,53-59,62,63,65,66,68,69 and 71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-4,13-15,49-52,60,61 and 70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 17 January 2007 has been entered.

Claims 1, 12, 64 and 67 have been cancelled. Claims 2-11, 13-63, 65, 66 and 68-71 are pending. Claims 5-11, 16-48, 53-59, 62, 63, 65, 66, 68, 69 and 71 are withdrawn. Claims 2-4, 13-15, 49-52, 60, 61 and 70 are under final rejection.

Response to Arguments

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 2-4, 14, 15, 49-52, 60, 61, and 70 under 35 U.S.C. §103(a) as being obvious over Shepard *et al.* (2000, April) in view of Grovit-Ferbas *et al.* (2000, July, IDS filed on 24 April 2006) is **maintained** for reasons of record.

The instant claims are directed to a composition comprising a purified nonpathogenic microorganism suspended in a liquid matrix; and a kit comprising the composition.

Examiner's rejection in the Action mailed on 14 July 2006 is as follows:

Shepard *et al.* teach amplification of HIV-1 RNA in blood, cerebral spinal fluid, saliva, breast milk, seminal plasma, and cervical-vaginal lavage fluid (Abstract). Shepard *et al.* do not teach purifying nonpathogenic microorganisms by covalent attachment of a compound to surface proteins.

Grovit-Ferbas *et al.* teach chemical inactivation of HIV-1 (Abstract) in formaldehyde and virus purification by ultrafiltration (p.5803, Fractionation of virion-bound and soluble gp120 and Fractionation of virus on Percoll gradient). Grovit-Ferbas *et al.* further teach that this inactivation method is used alone or in combination with the thermal treatment. See page 5808, left column, second to last paragraph.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the virus sample of Shepard *et al.* by inactivating the virus-containing biological sample with the chemical treatment as taught by Grovit-Ferbas *et al.* The skilled artisan would have been motivated to do so to create a safe nonpathogenic positive control sample. There would have been a reasonable expectation of success, given that the chemical treatment inactivates HIV-1 by at least 7 logs and still associates with envelope through purification by ultrafiltration, as taught by Grovit-Ferbas *et al.* Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Applicants argue the following: (1) Shepart *et al.* does not provide a composition comprising a purified virus that has been rendered non-pathogenic by covalent linkage with a compound having functional groups; (2) the emphasis in Grovit-Ferbas is on maintaining the integrity of surface proteins while reducing the infectivity, which would not suggest to one skilled in the art that the nucleic acids would be left intact enough so as to be amenable to amplification; (3) the process in Grovit-Ferbas is a combination of formaldehyde treatment and thermal treatment; (4) the composition as recited in claim 2 can be stored at 2-8°C (page 14, lines 29-30) and yet maintain its ability to serve as a

positive control material. Applicant's arguments have been fully considered but are not persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Examiner agrees with the Applicants on the missing elements of disclosure in Shepard *et al.*, which was stated in the previous Office Action (see above). However, the limitation of a purified nonpathogenic virus made by chemical treatment is described in Grovit-Ferbas on 5803, left column.

Applicants' contention of the emphasis in Grovit-Ferbas is irrelevant to the claimed invention, so long as the reference teaches the limitations in the instant claims. Applicants' assertion that there is suggestion of intact amplifiable nucleic acid lacks evidentiary basis. The rationale behind the chemical treatment is the modification of viral surface proteins so as to prevent the modified viruses from binding to host cells. The nucleic acid inside the viral particles would be protected by the maintained surface proteins and hence intact enough for amplification. Grovit-Ferbas *et al.* describe two methods, thermal and formaldehyde treatments, which can be used alternatively or in combination, as suggested in the last two paragraphs. Furthermore, the claim as written does not exclude the thermal treatment and limit to only the chemical treatment. Therefore, the disclosure by Grovit-Ferbas *et al.* meets the limitations in the claimed invention.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, one skilled in the art would be motivated to modify the positive control of Shepard *et al.* by replacing with the chemically modified virus of Grovit-Ferbas *et al.* to improve the positive control, so that the structure of the nonpathogenic positive-control virus more closely resembles that of the test virus, which would be a better reference with more similar amplification conditions and generate similar number of copies of nucleic acid as the test virus.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the composition can be stored at 2-8°C and yet maintain its ability to serve as a positive control material) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The rejection of claims 2-4, 13-15, 49-52, 60, 61, and 70 under 35 U.S.C. §103(a) as being obvious over Shepard *et al.* (2000, April) in view of Grovit-Ferbas *et al.* (2000, July, IDS filed on 24 April 2006) is **maintained** for reasons of record.

The instant claims have a further limitation of modifying the liquid matrix to render it suitable for lyophilization.

Examiner's rejection in the Action mailed on 14 July 2006 is as follows:

The relevance of Shepard *et al.* and Grovit-Ferbas *et al.* is set forth above. Neither reference teaches the preparation of the liquid matrix for lyophilization.

Norman *et al.* teach the preservation of microorganisms by adding to the suspending fluid of sucrose to a final concentration of 12% volume-by-volume (p.69, right column, line no. 8-14).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the virus sample of Shepard *et al.* by inactivating the virus-containing biological sample with the chemical treatment as taught by Grovit-Ferbas *et al.* and by adding sucrose as suggested by Norman *et al.* The skilled artisan would have been motivated to do so for the ease of handling and transporting lyophilized samples as well as long term storage and stability. There would have been a reasonable expectation of success, given that the sucrose-lyophilized samples enhance the recovery of freeze-dried microorganisms, as taught by Norman *et al.* Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Applicants argue that in the reference of Norman *et al.*, the microorganisms were not rendered non-pathogenic. However, the non-pathogenic microorganisms are described by Grovit-Ferbas *et al.* as set forth above. Norman *et al.* is cited to meet the limitation of modifying the liquid matrix for lyophilization. Applicant's arguments have been fully considered but are not persuasive.

Conclusion

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE**

FINAL even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Contact Information

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Jeffrey Parkin, Ph.D.
Primary Examiner
10 April 2007

Louise Humphrey, Ph.D.
Assistant Examiner